27 Craniofacial and Cardioteratogenic Effects of Nicotine in Mouse Embryos

Fazel , A.R. , Department of Anatomy , Mashhad University of Medical Sciences , Mashhad Iran

During the past few decades, it has become increasingly evident that human embryos are subject to a variety of enviromental influences that might have deleterious effects on their development. these enviromental agents can alter the normal course of embryogenesis. In this investigation, effects of nicotine on heart and craniofacial development in mouse embryos from early days of gestation through the first few post natal days was studied by means of histochemical and scanning electron microscopy methods. We were able to produce a spectrum of craniofacial defects (cleft lip with or without related cleft of palate , CL/P) and cardiac malformations(endocardial cushion type of defects) by exposing the mother to nicotine or smoke from high nicotine cigarettes, NIH code 32,. The critical time of development was determined and nicotine was injected intraperitoneally at different concentrations. The dosage of 1 mg/kg of nicotine on the morning of gestational day 10 (11:00 a.m.) was the most effective and was used for the greater part of this research. All doses were administered in a volume of 25 Ul. Controls were injected with an equal volume of diluent (sterile o.9% NaCl). Day 10 of gestetion (vaginal plug =day 0) is prior to the time that mesenchymal cells migrate into the cardiac jelly (CJ) of the endocardial cushions just before the cardiac septa develop.
Intrapritoneal injection of 1 mg/kg of nicotine, produced 32% (47/148) of embryos or newborns with cardiac defects and 20% (30/148) of these also showed CL/P. When mesenchymal cells of the CJ and the facial processes were examined two days after nicotine exposure, striking changes in cell shape and size were evident.In-as-much as the incidence of mesenchymal changes in the CJ and in the mesenchyme of the facial placodes seen at day 12 (two days after exposure of nicotine) parallels the incidence of malformations seen in newborns. It appears that the change morphology of these cells may reflects a failure of normal tissue interactions. It is possible that nicotine affects the glycosaminoglycans (GAG)a prominent class of extra cellular matrix macromolecules which are important in many developmental phenomena such as cellular interactions , cell shape , differentiation, etc. We also conclude that critical stages of development occur in the heart,facial processes at the same time and therefore certain teratogens such as nicotine may interfere with normal development of several organ systems concurrently.